

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (currently amended) A composition comprising a first oligomer and a second oligomer, wherein:

at least a portion of said first oligomer is capable of hybridizing with at least a portion of said second oligomer,

one of said oligomers is an antisense strand and the other of said oligomers is a sense strand, said oligomers are not covalently linked, and each of said oligomers is from about 12 to about 30 linked nucleosides in length;

at least a portion of said first oligomer is complementary to and capable of hybridizing with a selected target nucleic acid, and

~~at least one each~~ of said first ~~or~~ and said second oligomers includes at least one sugar surrogate wherein said sugar surrogate is a 4'-thioribonucleoside or a 2'-deoxy-4'-thioribonucleoside.

2-6. (canceled)

7. (original) The composition of claim 1 wherein said first oligomer is an antisense oligomer.

8. (original) The composition of claim 7 wherein said second oligomer is a sense oligomer.

9. (original) The composition of claim 7 wherein said second oligomer has a plurality of ribose nucleoside units.

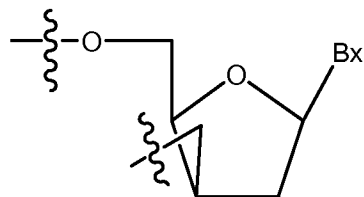
10. (canceled)

11. (withdrawn) The composition of claim 1 wherein the sugar surrogate is a cyclobutyl nucleoside, cyclopentyl nucleoside, proline nucleoside, cyclohexene nucleoside, hexose nucleoside or a cyclohexane nucleoside.

12. (canceled)

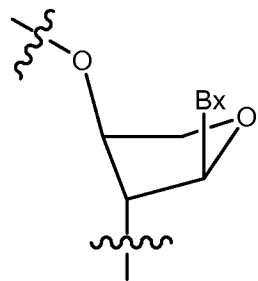
13. (withdrawn) The composition of claim 12 wherein the sugar surrogate is an arabinonucleoside.

14. (withdrawn) The composition of claim 12 wherein the sugar surrogate is an xylonucleoside of the formula:



where Bx is a heterocyclic base moiety.

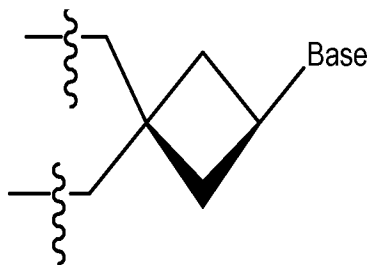
15. (withdrawn) The composition of claim 12 wherein the sugar surrogate is a threonenucleoside of the formula:



wherein Bx is a hetrocyclic base moiety.

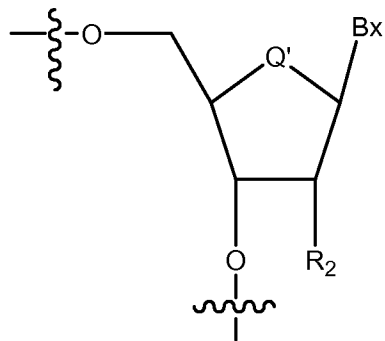
16. (withdrawn) The composition of claim 11 wherein the sugar surrogate is a cyclobutyl nucleoside.

17. (withdrawn) The composition of claim 16 wherein the cyclobutyl nucleoside is of the formula:



18. (withdrawn) The composition of claim 11 wherein the sugar surrogate is a cyclopentyl nucleoside.

19. (withdrawn) The composition of claim 18 wherein the cyclopentyl nucleoside is of the formula:



where:

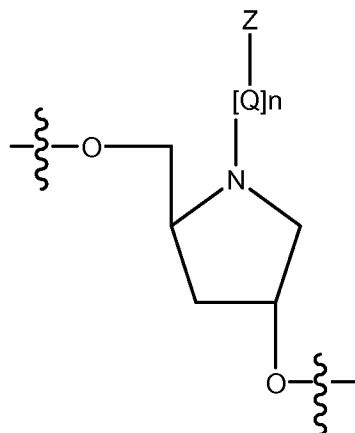
Bx is a heterocyclic base moiety;

Q' is CH₂, CHF, or CF₂; and

R₂ is sugar substituent.

20. (withdrawn) The composition of claim 11 wherein the sugar surrogate is a proline nucleoside.

21. (withdrawn) The composition of claim 20 wherein the proline nucleoside is of the formula:



wherein:

Z is L_8 , L_8-G_1 , L_9 , L_9-G_2 , $NR_{23}R_{24}$, a nitrogen-containing heterocycle, a purine, a pyrimidine, a phosphate group, a polyether group, or a polyethylene glycol group;

L_8 is C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, or C_2 - C_{20} alkynyl;

L_9 is C_6 - C_{14} aryl or C_7 - C_{15} aralkyl;

G_1 is halogen, OR_{21} , SR_{22} , $NR_{23}R_{24}$, $C(=NH)NR_{23}R_{24}$, $NHC(=NH)NR_{23}R_{24}$, $CH=O$, $C(=O)OR_{25}$, $CH(NR_{23}R_{24})(C(=O)OR_{25})$, $C(=O)NR_{23}R_{24}$, a metal coordination group, or a phosphate group;

G_2 is halogen, OH, SH, SCH_3 , or $NR_{23}R_{24}$;

R_{21} is H, C_1 - C_6 alkyl, or a hydroxyl protecting group;

R_{22} is H, C_1 - C_6 alkyl, or a thiol protecting group;

R_{23} and, R_{24} are, independently, H, C_1 - C_6 alkyl, or an amine protecting group;

R_{25} is H, C_1 - C_6 alkyl, or an acid protecting group;

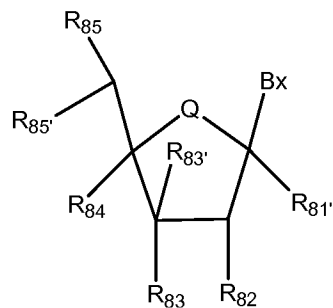
Q is L_1 , G_3 , L_1-G_3 or $G_3-L_1-G_3$;

L_1 is C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, or C_2 - C_{20} alkynyl;

G_3 is $C(=O)$, $C(=S)$, $C(O)--O$, $C(O)--NH$, $C(S)--O$, $C(S)--NH$ or $S(O)_2$; and

n is 0 or 1.

22. (withdrawn) The composition of claim 1 wherein the sugar surrogate is of the formula:



where:

Bx is a heterocyclic base moiety;

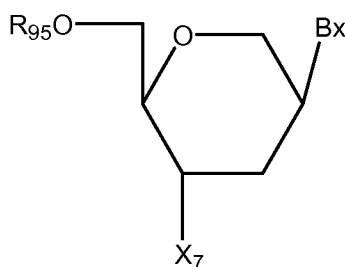
Q is S, O, NH, N(C₁-C₆ alkyl), CH₂, CHF, or CF₂;

R₈₂ is a sugar substituent;

R₈₃ and R₈₅ are each independently OH, a protected hydroxyl group, an internucleoside linkage to an adjacent monomer, or a terminal group; and

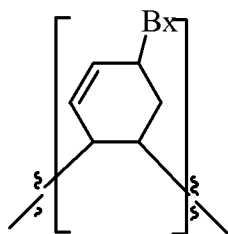
R₈₁, R₈₃, R₈₄ and R₈₅ are each independently H, alkyl, aralkyl, or aryl.

23. (withdrawn) The composition of claim 11 wherein the sugar surrogate is of formula:



wherein Bx is a heterocyclic nucleobase, R₉₅ is H, a hydroxyl protecting group, an internucleoside linkage to an adjacent monomer, or a terminal group, and X₇ is a H or a sugar substituent.

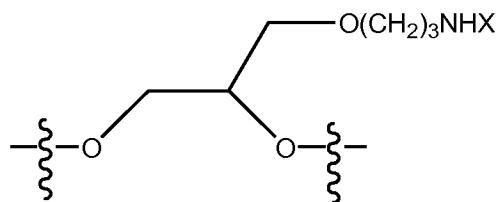
24. (withdrawn) The composition of claim 11 wherein the sugar surrogate is of the formula:



wherein Bx is a heterocyclic base moiety.

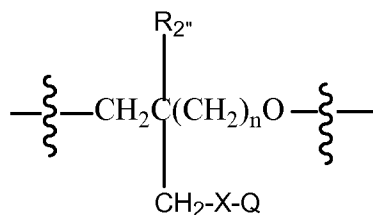
25. (canceled)

26. (withdrawn) The composition of claim 1 wherein the sugar surrogate comprises at least one monomer of the formula:



wherein X is a conjugate.

27. (withdrawn) The composition of claim 1 wherein the oligomer comprises at least one monomer of the formula:



wherein:

$R_{2''}$ is hydrogen, nitro, lower alkyl amino, diloweralkyl amino or methyl;

X is oxygen, sulfur, or $-NR_{6''}$;

$R_{6''}$ is hydrogen or lower alkyl;

n is an integer from 1 to 40;
Q is a heterocyclic base moiety.

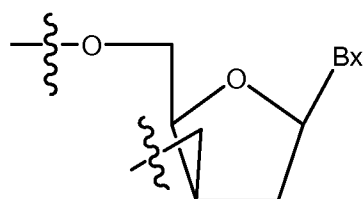
28-35. (canceled)

36. (withdrawn) The composition of claim 28 wherein the sugar surrogate is a cyclobutyl nucleoside, cyclopentyl nucleoside, proline nucleoside, cyclohexene nucleoside, hexose nucleoside or a cyclohexane nucleoside.

37. (canceled)

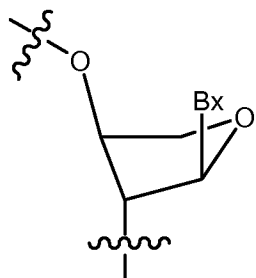
38. (withdrawn) The composition of claim 37 wherein the sugar surrogate is an arabinonucleoside.

39. (withdrawn) The composition of claim 37 wherein the sugar surrogate is an xylonucleoside of the formula:



where Bx is a heterocyclic base moiety.

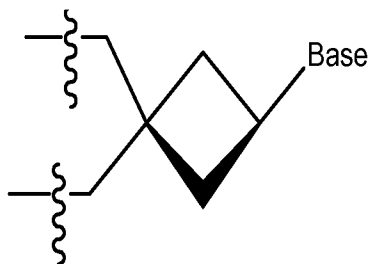
40. (withdrawn) The composition of claim 37 wherein the sugar surrogate is a threonucleoside of the formula:



wherein Bx is a hetrocyclic base moiety.

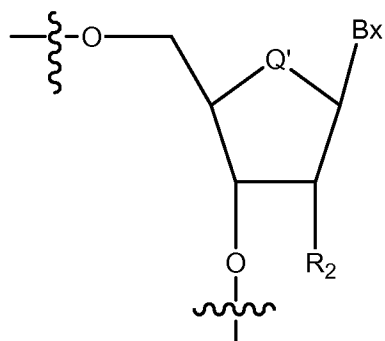
41. (withdrawn) The composition of claim 36 wherein the sugar surrogate is a cyclobutyl nucleoside.

42. (withdrawn) The composition of claim 41 wherein the cyclobutyl nucleoside is of the formula:



43. (withdrawn) The composition of claim 36 wherein the sugar surrogate is a cyclopentyl nucleoside.

44. (withdrawn) The composition of claim 43 wherein the cyclopentyl nucleoside is of the formula:



where:

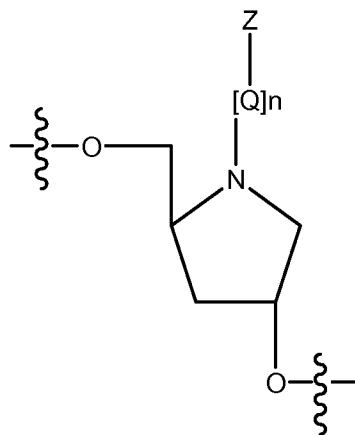
Bx is a heterocyclic base moiety;

Q' is CH₂, CHF, or CF₂; and

R₂ is OH; F; O-, S-, or N-alkyl; O-, S-, or N-alkenyl; O-, S- or N-alkynyl; or O-alkyl-O-alkyl, wherein the alkyl, alkenyl and alkynyl may be substituted or unsubstituted C₁ to C₁₀ alkyl or C₂ to C₁₀ alkenyl or alkynyl.

45. (withdrawn) The composition of claim 36 wherein the sugar surrogate is a proline nucleoside.

46. (withdrawn) The composition of claim 45 wherein the proline nucleoside is of the formula:



wherein:

Z is L₈, L₈-G₁, L₉, L₉-G₂, NR₂₃R₂₄, a nitrogen-containing heterocycle, a purine, a pyrimidine, a phosphate group, a polyether group, or a polyethylene glycol group;

L₈ is C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, or C₂-C₂₀ alkynyl;

L₉ is C₆-C₁₄ aryl or C₇-C₁₅ aralkyl;

G₁ is halogen, OR₂₁, SR₂₂, NR₂₃R₂₄, C(=NH)NR₂₃R₂₄, NHC(=NH)NR₂₃R₂₄, CH=O, C(=O)OR₂₅, CH(NR₂₃R₂₄)(C(=O)OR₂₅), C(=O)NR₂₃R₂₄, a metal coordination group, or a phosphate group;

G₂ is halogen, OH, SH, SCH₃, or NR₂₃R₂₄;

R₂₁ is H, C₁-C₆ alkyl, or a hydroxyl protecting group;

R₂₂ is H, C₁-C₆ alkyl, or a thiol protecting group;

R₂₃ and, R₂₄ are, independently, H, C₁-C₆ alkyl, or an amine protecting group;

R₂₅ is H, C₁-C₆ alkyl, or an acid protecting group;

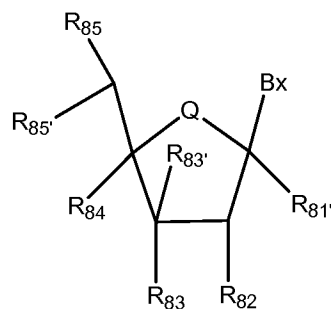
Q is L₁, G₃, L₁-G₃ or G₃-L₁-G₃;

L₁ is C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, or C₂-C₂₀ alkynyl;

G₃ is C(=O), C(=S), C(O)--O, C(O)--NH, C(S)--O, C(S)--NH or S(O)₂; and

n is 0 or 1.

47. (withdrawn) The composition of claim 28 wherein the sugar surrogate is of the formula:



where:

Bx is a heterocyclic base moiety;

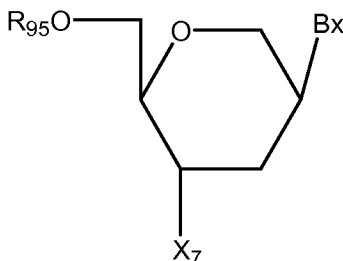
Q is S, O, NH, N(C₁-C₆ alkyl), CH₂, CHF, or CF₂;

R₈₂ is a sugar substituent;

R₈₃ and R₈₅ are each independently OH, a protected hydroxyl group, an internucleoside linkage to an adjacent monomer, or a terminal group; and

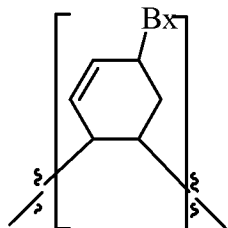
R₈₁', R₈₃', R₈₄ and R₈₅' are each independently H, alkyl, aralkyl, or aryl.

48. (withdrawn) The composition of claim 36 wherein the sugar surrogate is of formula:



wherein Bx is a heterocyclic nucleobase, R₉₅ is H, a hydroxyl protecting group, an internucleoside linkage to an adjacent monomer, or a terminal group, and X₇ is a H or a sugar substituent.

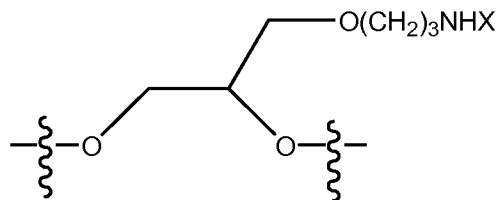
49. (withdrawn) The composition of claim 36 wherein the sugar surrogate is of the formula:



wherein Bx is a heterocyclic base moiety.

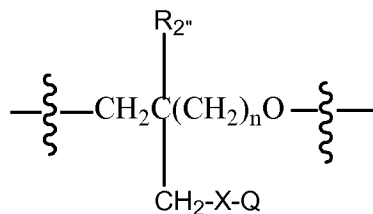
50. (withdrawn) The composition of claim 36 wherein the sugar surrogate is a 4'-thioribonucleoside or a 2'-deoxy-4'-thioribonucleoside.

51. (withdrawn) The composition of claim 28 wherein the sugar surrogate comprises at least one monomer of the formula:



wherein X is a conjugate.

52. (withdrawn) The composition of claim 28 wherein the sugar surrogate comprises at least one monomer of the formula:



wherein:

R_{2''} is hydrogen, nitro, lower alkyl amino, diloweralkyl amino or methyl;

X is oxygen, sulfur, or --NR_{6''} ;

R_{6''} is hydrogen or lower alkyl;

Q is a heterocyclic base; and

n is an integer from 1 to 40.

53-58. (canceled)

59. (currently amended) A ~~pharmaceutical~~ composition comprising the composition of claim 1 and a pharmaceutically acceptable carrier.

60-61. (canceled)

62. (currently amended) A method of ~~modulating~~ decreasing the expression of a target nucleic acid in a cell *in vitro* comprising contacting said cell with a composition of claim 1.

63-67. (canceled)

DOCKET NO.: ISIS-5207

PATENT

Application No.: 10/701,236

Office Action Dated: October 2, 2006

68. (new) The composition of claim 1 wherein said first oligomer has a region of at least 17 contiguous nucleosides that is 100% complementary to a region of at least 17 contiguous nucleosides located on said second oligomer.